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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,606	03/28/2006	Jo Klaveness	PN0368	6864

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GE HEALTHCARE, INC.
IP DEPARTMENT
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EXAMINER	
PERREIRA, MELISSA JEAN	
ART UNIT	**PAPER NUMBER**
1618	

MAIL DATE	DELIVERY MODE
09/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/573,606	KLAVENESS ET AL.	
	Examiner	Art Unit	
	Melissa Perreira	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,15-18 and 20-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,15-18 and 20-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 13,15-18 and 20-24 are pending in the application. Any objections and/or rejections from previous office actions that have not been reiterated in this office action are obviated.

Terminal Disclaimer

1. The terminal disclaimers filed on 9/12/07 disclaiming the terminal portion of any patent granted on this application have been accepted. The terminal disclaimers have been recorded.

New Grounds of Rejection Necessitated by the Amendment

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 13,15-18 and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maten et al. (*Gastroenterol.* **2002**, *122*, 406-414) in view of Klaveness et al. (US 6,610,269B1) and further in view of Waggoner et al. (US 6,008,373).

3. Maten et al. (*Gastroenterol.* **2002**, *122*, 406-414) discloses cathepsin B sensing NIR fluorochrome probes comprising Cy5.5 (cyanine dye) containing cleavage sites, and a partially pegylated poly-L-lysine for imaging of the colon (p408, paragraph 3; figure 2). Colonic adenomas can be visualized after injection of the NIRF probe into a

mouse (figure 5) and colonic adenomatous polyps ultimately lead to carcinoma formation and their detection has been shown to reduce the incidence of colorectal cancer. The probes are nonfluorescent in their native state but upon enzymatic cleavage the agent becomes fluorescent in the near-IR (figure 1; p412, paragraph 2). Maten et al. does not disclose the contrast agent of the disclosure having a molecular weight of below 10,000 daltons.

4. Klaveness et al. (US 6,610,269B1) discloses contrast agents of formula V-L-R where V is a vector moiety (i.e. peptide or non-peptide), L is a linker moiety (i.e. PEG) and R is a detectable reporter moiety/moieties (i.e. cyanine dye) (column 4, lines 10-20; column 5, lines 23-25; column 24, lines 56-58; column 28, lines 65+; column 42, line 40). The linker moiety may contain 2-100 recurring units of ethylene oxide, have a molecular weight between 120 D to 20 kDa (column 33, line 1; column 36, lines 62-64) and also contain a biodegradable function which on breakdown can release the reporter from the vector (column 36, lines 14-18). The contrast agents of the disclosure are used for in vivo imaging of diseases associated with angiogenesis, such as colorectal cancer via administration with a physiologically acceptable carrier (column 3, line 27; column 4, line 53; column 56, lines 18-20).

5. Waggoner et al. (US 6,008,373) discloses that low molecular weight fluorescent labeling complexes/probes containing cyanine dyes, linkers and proteins have enhanced cell penetrating capabilities (abstract; column 2, lines 38-43). The fluorescent labeling complexes/probes having greater penetration into cellular environments have molecular weights of 500 to 10000 Daltons (column 6, lines 15-22).

6. It is respectfully pointed out that instant claim 23 is a product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

7. At the time of the invention it would have been obvious to one ordinarily skilled in the art to minimize the molecular weight of the fluorochrome probes of Maten et al. to about 500 to 10000 Daltons by minimizing the linker molecular weight or the number of detectable reporter moieties to provide for probes having greater penetration into cellular environments. The probes of the combined disclosures are useful for imaging the colon as they can provide for real time imaging that may have a significant impact on diagnosis of a very early stage of intestinal disease (Maten et al. p414, paragraph 4).

8. Claims 13,15-18 and 20-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weissleder et al. (*Nature Biotech.* **1999**, *17*, 375-378) in view of Klaveness et al. (US 6,610,269B1) and further in view of Waggoner et al. (US 6,008,373).

9. Weissleder et al. (*Nature Biotech.* **1999**, *17*, 375-378) discloses NIRF probes for in vivo imaging comprising poly-L-lysine, MPEG and Cy5.5 (cyanine dye) (abstract; p375, paragraph 4). The NIRF probes of the disclosure are enzymatically activatable,

thus producing fluorescence upon enzymatic cleavage (p375, paragraphs 2, 4 and 5). The NIRF probes were internalized into colon adenocarcinoma via uptake through fluid phase endocytosis thus indicating the feasibility of using these for the detection of primary tumors in the colon, such as colon cancer (p376, paragraph 1; p377, paragraph 1).

10. Klaveness et al. (US 6,610,269B1) discloses contrast agents of formula V-L-R where V is a vector moiety (i.e. peptide or non-peptide), L is a linker moiety (i.e. PEG) and R is a detectable reporter moiety/moieties (i.e. cyanine dye) as well as that stated above.

11. Waggoner et al. (US 6,008,373) discloses that low molecular weight fluorescent labeling complexes/probes containing cyanine dyes, linkers and proteins have enhanced cell penetrating capabilities (abstract; column 2, lines 38-43). The fluorescent labeling complexes/probes having greater penetration into cellular environments have molecular weights of 500 to 10000 Daltons (column 6, lines 15-22).

12. It is respectfully pointed out that instant claim 23 is a product-by-process limitations. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

13. At the time of the invention it would have been obvious to one ordinarily skilled in the art to minimize the molecular weight of the fluorochrome probes of Weissleder et al. to about 500 to 10000 Daltons by minimizing the linker molecular weight or the number of detectable reporter moieties to provide for probes having greater penetration into cellular environments. The probes of the combined disclosures are advantageous for imaging the colon as they can be in the detection of the early stage tumors in vivo (Weissleder et al., abstract).

Conclusion

No claims are allowed at this time.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Melissa Perreira whose telephone number is 571-272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MP
September 17, 2007

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER